

45. The method of claim 44 in which the composition comprises rough, complete-core lipopolysaccharide (LPS) antigen of at least two of the following gram negative bacterium: *E. coli*; *Pseudomonas*; *Klebsiella*; *Salmonella* and *Bacteroides*.

46. The method of claim 45 in which the composition comprises rough, complete-core lipopolysaccharide (LPS) antigen of at least *E. coli*; *Pseudomonas*; and *Bacteroides*.

sub B2 > 47. The method of claim 44 in which the composition comprises killed whole cells.

48. The method of claim 47 in which the composition comprises killed whole *E. coli* K12, containing rough complete-core LPS antigen.

49. The method of claim 45 in which the composition comprises a cocktail of killed Ra chemotype whole-cell mutants of at least three of the following species of gram-negative bacteria: *E. coli* K12, *E. coli* R1, *Bacteroides fragilis*, *Pseudomonas aeruginosa*.

A2 cm 50. The method of claim 49 in which the composition comprises killed whole-cell Ra LPS mutants from each of the following species of gram-negative bacteria: *E. coli* K12, *E. coli* R1, *Bacteroides fragilis*, *Pseudomonas aeruginosa*.

sub B3 > 51. The method of claim 44 in which the composition comprises purified detoxified Ra LPS conjugated to protein.

52. The method of claim 51 in which the Ra LPS conjugate is conjugated *E. coli* K12 Ra LPS.

53. The method of claim 51 in which the composition comprises a cocktail of Ra LPS from multiple species of gram-negative bacteria, conjugated to a protein.

54. The method of claim 53 in which the composition comprises conjugates of Ra LPSs from at least three of the following species of gram-negative bacteria: *E. coli* K12, *E. coli* R1, *Bacteroides fragilis*, *Pseudomonas aeruginosa*.

55. The method of claim 53 in which the composition comprises Ra LPS incorporated in a liposome.

56. The method of claim 55 in which the composition comprises *E. coli* K12 Ra LPS in a liposome.

sub B4 > 57. The method of claim 55 in which the composition comprises a cocktail of Ra LPSs from multiple species of gram-negative bacteria incorporated in liposomes.

58. The method of claim 57 in which the cocktail comprises Ra LPSs from at least three of the following species of gram-negative bacteria: *E. coli* K12, *E. coli* R1, *Bacteroides fragilis*, and *Pseudomonas aeruginosa*.

59. The method of claim 44 in which the composition comprises rough, complete-core lipopolysaccharide (LPS) antigen of *E. coli* K12.

60. The method of claim 59 in which the composition further comprises rough, complete-core lipopolysaccharide (LPS) antigen of a second bacteria other than *E. coli* K12.

svb B5 61. The method of claim 60 in which the animal is a mammal.

62. The method of claim 61 in which the animal is a human patient.

63. The method of claim 59 in which the composition comprises LPS of an Ra rough *E. coli* K12.

A2 svb B6 64. The method of claim 60 in which the second bacterium is an *E. coli* or a *Salmonella* bacterium.

svb 65. The method of claim 60 in which the second bacteria is a *Bacteroides*.

svb B7 66. The method of claim 60 in which the composition comprises complete-core, rough, LPS antigen from a third Gram-negative bacterium different from the first and from the second Gram-negative bacterium.

67. The method of claim 66 in which the composition comprises complete-core, rough, LPS antigen from a fourth Gram-negative bacterium different from each of the first, the second, and the third Gram-negative bacteria.

68. The method of claim 59 in which the second Gram-negative bacterium is *E. coli* R1.

69. The method of claim 59 in which the second Gram-negative bacterium is a *Salmonella* bacterium.

70. The method of claim 66 in which the second bacterium is a *Klebsiella* and third bacterium is a *Pseudomonad*.

71. The method of claim 67 in which the second bacterium is a *Klebsiella*, the third bacterium is a *Pseudomonad*, and the fourth bacterium is a *Bacteroides*.

svb B8 72. The method of claim 64 or claim 69 in which the *Salmonella* bacterium is *Salmonella minnesota*.

73. The method of claim 67 in which complete core antigen from each of the four bacteria is present in generally equal amounts by weight.

74. The method of claim 66 in which the composition comprises LPS antigens from at least two different Gram-negative bacterial strains of the same species.

75. The method of claim 59 in which the antigen causes the patient to produce an antibody that binds to an epitope in the core region of the LPS of at least one Gram-negative bacterial strain whose LPS is not part of the composition.

76. The method of claim 75 in which the patient's antibody binds to the LPS of at least one smooth Gram negative bacterial strain.

77. The method of claim 75 in which the composition comprises the antigen in a liposome.

78. The method of claim 77 in which the ratio (weight:weight) of lipid in the liposome to the LPS antigen is between 1:1 and 5000:1.

79. The method of claim 77 in which the ratio (weight:weight) is between 10:1 and 1000:1.

80. The method of claim 77 in which the liposome comprises a component selected from the group consisting of: phospholipid, cholesterol, positively charged compounds, negatively charged compounds, amphipathic compounds.

81. The method of claim 77 in which the liposome is a multilamellar type liposome (MLV).

82. The method of claim 77 in which LPS in the acid salt form is incorporated into the liposome.

83. The method of claim 77 in which the liposome is a small or large unilamellar liposome (SUVs and LUVs).

84. The method of claim 59 in which the composition is administered intramuscularly, intravenously, subcutaneously, intraperitoneally, via the respiratory tract, or via the gastrointestinal tract.

85. The method of claim 59 in which the dose of antigen is over 0.01 ng per kilogram of patient body weight.

86. The method of claim 85 in which the dose is less than 1000ng per kilogram of patient body weight.

87. The method of claim 85 in which the dose is less than 100 micrograms per kilogram of patient body weight.

88. The method of claim 59 in which the composition is administered in multiple doses, the first of which is administered at least 2 days prior to potential endotoxin exposure.

89. The method of claim 59 in which the antigen is present in a killed bacterium.

90. The method of claim 59 in which the antigen is separated from the bacterium.

91. The method of claim 59 in which the antigen is chemically detoxified.

92. The method of claim 59 or claim 90 in which the bacterium is genetically engineered.

93. The method of claim 59 in which the composition further comprises an adjuvant.

94. The method of claim 93 in which the adjuvant is alum.

95. A vaccine composition for reducing the adverse effects of endotoxemia in a human patient which comprises an effective amount of a composition comprising purified complete core rough lipopolysaccharide antigen of *E. coli* K12, said composition further comprising liposomes which contain the antigen.

96. A method of reducing adverse effects of endotoxin in a warm-blooded animal, which method comprises administering to the warm-blooded animal an effective amount of a composition comprising rough lipopolysaccharide (LPS) antigen of a Gram-negative bacterium, said LPS antigen comprising the component of an *E. coli* Rb chemotype LPS, or the equivalent thereof in another species.

97. A method of quantitating lipopolysaccharide incorporated into liposomes by performing periodic acid/Schiff base staining.

98. The method of claim 97 in which the test is performed on a vaccine lot intended for clinical use.

99. A method of reducing adverse effects of endotoxin in a warm-blooded animal, which method comprises administering to the warm-blooded animal an effective amount of antibody produced by immunization with a composition according to claim 44 or claim 59.

Srb  
B12

A2  
cm  
003240-945450